Amendments to the Specification:

At page 31, please replace lines 2-5 with the following amended paragraph:

~~Figure 12 depicts~~ Figures 12A-12D depict graphs demonstrating the lack of effect of HN and structural derivatives thereof on neuronal death induced by polyglutamine repeat Q79. Mean ±S.D. values of three independent experiments are indicated in the graphs.

At page age 31, please replace lines 6-12 with the following amended paragraph:

~~Panel A~~: Figure 12A demonstrates the lack of the effect of pHN, pHNG, or pHNA on neuronal death caused by the expression of Q79 induced by ecdysone. F11/EcR cells were transfected with ecdysone-inducible type Q79 expression plasmid, and empty vector (pFLAG), pHN, pHNG, or pHNA, and were cultured for 72 hours in the presence (+) or absence (-) of ecdysone. Cell death was measured by trypan blue exclusion assay.

At page 31, please replace lines 13-19 with the following amended paragraph:

~~Panel B:~~ Figure 12B demonstrates a significant suppressive effect by pHN co-transfection on neuronal death caused by ecdysone-induced expression of NL-APP, V6421 APP, M146L PS-1, or N141I PS-2. Under the same conditions as in ~~Panel A~~ Figure 12A, F11/EcRcells were transfected with ecdysone-inducible FAD gene plasmid, and pFLAG or pHN, and then, were cultured for 72 hours in the presence (+) or absence (-) of ecdysone. Cell death was measured by trypan blue exclusion assay.

At page 31, please replace lines 20-26 with the following amended paragraph:

~~Panel C:~~ Figure 12C demonstrates the lack of effects of sHN, sHNG, or sHNA on neuronal death induced by ecdysone-inducible expression of Q79. F11/EcR cells were transfected with ecdysone-inducible Q79 plasmids; treated with 1 μM sHN, sHNG, or sHNA; and then, were cultured in the presence (+) or absence (-) of ecdysone. 72 hours after the initiation of the exdysone treatment, cell death was measured by trypan blue exclusion assay.

At page 31, please replace lines 27-34 with the following amended paragraph:

~~Panel D:~~ Figure 12D demonstrates a significant suppressive effect by sHN on neuronal death caused by ecdysone-induced expression of NL-APP, V642I APP, M146L PS-1, or N141I PS-2. Under the same conditions as in ~~Panel C~~ Figure 12C, F11/EcR cells were transfected with ecdysone-inducible FAD gene plasmid; treated with 1μM sHN; and then, were cultured in the

presence (+) or absence (-) of ecdysone. 72 hours after the initiation of the ecdysone treatment, cell death was measured by trypan blue exclusion assay.

At page 31, lines 35-36 and Page 31, lines 1-2, please replace with the following amended paragraph:

~~Figure 13 depicts~~ Figures 13A-13B depict graphs demonstrating the lack of the effect of HN and structural derivatives thereof on neuronal death induced by the ALS-associated SOD1 mutants. Mean ±S.D. values of three independent experiments are indicated in the graphs.

At page 32, please replace lines 3-8 with the following amended paragraph:

~~Panel A:~~ Figure 13A demonstrates the lack of the effect of pHN co-transfection on neuronal death induced by the expression of the ALS-related SOD1 mutants. F11 cells were trans£ected with pEF-BOS encoding the ALS-associated mutant SOD1 (A4T, G85R, or G93A mutants' of SOD1) and empty vector (pFLAG) or pHN. Cell death was measured by trypan blue exclusion assay.

At page 32, please replace lines 9-13 with the following amended paragraph:

~~Panel B:~~ Figure 13B demonstrates the lack of the effect of sHN, sHNG, or sHNA on neuronal death induced by the expression of the ALS-associated SOD1 mutants. F11 cells were transfected with pEF-BOS encoding A4T , G85R, or G93A SOD1, and were treated with 100 μM sHN, sHNG, or sHNA. Cell death was then measured by trypan blue exclusion assay.

At page 34, please replace lines 7-18 with the following amended paragraph:

~~Figure 19 depicts~~ Figures 19A-19D depict photographs demonstrating the expression of HN mRNA in various human tissues. Radiolabeled antisense HN (panel a), 19mer encoding the 5' region (panel b), or DT77 (panel c) was hybridized as a probe to the sheet blotted with human tissue polyA-RNA (lane 1: brain; lane 2: heart; lane 3: skeletal muscles; lane 4: large intestine; lane 5: thymus; lane 6: spleen; lane 7: kidney; lane 8: liver; lane 9: small intestine; lane 10: pancreas; lane 11: lung; lane 12: peripheral leukocytes). The result of Northern blotting on the same sheet using β-actin as the probe is shown in panel d. The numbers on the left indicate molecular sizes. Similar experiments were performed at least three times, and similar results were obtained.

At page 37, please replace lines 16-27 with the following amended paragraph:

~~Figure 25 depicts~~ Figures 25A-25F depict graphs demonstrating the effect of AGA-HNG (SEQ ID NO: 60) on neuronal death induced by the four different types of FAD genes and Aβ1-43. Priamry cultured neurons were treated with 25 μM Aβ1-43 in the absence or presence at

various concentrations of AGA-HNG (panel B), or F11 cells were transfected with V642 I APP, NL-APP, M146L PS-1, or N141I PS-2 cDNA (panels C to F); and 72 hours later, cell death was measured by trypan blue exclusion assay. In the primary cultured neuron experiment using Aβ, various concentrations of HNG were used to perform similar experiments as controls. The result of untransfected cells is indicated as "no T"; and the result of cells transfected with the empty vector as "pcDNA". Mean:±S.D. values of three independent experiments are indicated in the graphs.

At page 47, please replace lines 19-30 with the following amended paragraph:

23 to 24 N-terminal residues of the entire 24 amino acids of the HN sequence satisfy the requirements necessary as a signal sequence (Nielsen, H. et al., 1999, Protein Eng. 12, 3-9; determination program provided at ~~<http://www.cbs.dtu.dk/services/SignalP/>~~ the SignalP World Wide Web server (CBS, the Technical University of Denmark)). The fact that intracellularly expressed HN is secreted into the culture media at micromolar concentrations suggests that HN has not a signal sequence activity itself, but has an activity similar to that of a signal sequence. Since the flag tag is positioned at the C-terminus, and the secreted HN polypeptide has a molecular weight concordant with the size expected for FLAG-fused HN, the entire HN sequence is suggested to encode a signal sequence-like secretion activity.

At page 50, lines 21-36, and page 51, lines 1-10, please replace with the following amended paragraph:

To elucidate the specificity of HN action, the ability of HN cDNA or HN polypeptide to antagonize cell death induced by causative genes of other neurodegenerative diseases was investigated. Polyglutamine Q79, having 72 repeats, is considered to be the cause of Huntington's disease (HD) and certain types of spinocerebellar ataxia (SCA) (Ikeda, H. etal. (1996) Nat. Genet. 13, 196-202; Kakizuka, A. (1997) Curro Opin. Neurol. 10, 28S-90). In accordance with the report that Q79 expression causes neuronal death, F11 cells underwent cell death due to the expression of Q79 ~~(Figure 12)~~ (Figures 12A-12D). Examination of neurotoxicity was carried out in the presence or absence of ecdysone by transfecting F11/EcR cells with Q79 plasmid, the expression of which is induced by ecdysone (pDN-E/GSH-Q79). In this system, cell mortality markedly increased in response to ecdysone treatment when F11/EcR cells were transfected with pDN-E/GSH-Q79 together with the empty vector (pFLAG) (Figure 12A). Similarly, high proportions of cell death of F11/EcR cells, transfected with pDN-E/GSH-Q79 together with pHN, pHNG, or pHNA, were induced by ecdysone treatment. Further, F11/EcR cell death caused by ecdysone-induced expression of any of the FAD gene was effectively suppressed by the co-transfection of pHN (Figure 12B). Cell death induced by Q79 was not suppressed in the experiment using sHN (Figure 12C). Extensive cell death was caused by ecdysone when F11/EcR cells were transfected with pDN-E/GSH-Q79, even in the presence of sHN, sHNG, or sHNA at a concentration of sHN or sHNG that enables complete suppression of F11/EcR cell death caused by anyone of the 4 types of FAD genes, just as in the absence of sHN, sHNG, or sHNA (Figure 12D).

At page 59, lines 24-36, and page 60, lines 1-6, please replace with the following amended paragraph:

Enhancement of the HNG action by mutation of HNG (S14G HN) was verified. According to an experiment, examining the neuroprotective action of HNGs wherein multiple amino acid residues are substituted with other amino acids, polypeptides with higher rescue activity compared to HNG were ~~obatined~~ obtained by mutating two positions, R4A/F6A (SEQ ID NO: 60). The polypeptide, dubbed AGA-HNG, not only completely rescued cell death of nerve cell line induced by FAD genes at a concentration as little as 0.1 nM, but completely rescued cell death of primary cultured neurons by Aβ at a concentration of 0.3 nM ~~(Figure 25)~~ Figures 25A-25F. Arg and Phe at position 4 and 6 of HNG, respectively, are positions which are cleaved by trypsine-like protease and chymotrypsin-like protease, respectively (see Figure 25A). Thus, it is likely that R4A/F6A substitution of HNG enhances resistance to degradation. A remarkable high activity for AGA-HNG is implied by the fact that AGA-HNG detoxifies the neurotoxicity of Aβ of high concentration, a 100000-fold higher concentration than AGA-HNG. Anti-AD agent that has such a broad spectrum with high neuroprotective action has not been reported so far. Application of AGA-HNG or derivatives thereof to chemotherapy of AD is expected.